# 論 文 要 旨

## Human Cathelicidin Antimicrobial Peptide LL-37 Promotes Lymphangiogenesis in Lymphatic Endothelial Cells through the ERK and Akt Signaling Pathways

Takahiro Yanagisawa, Masakazu Ishii*, Manami Takahashi, Kei Fujishima, Masahiro Nishimura

Molecular Biology Reports（IN PRESS）

LL-37, the only member of the cathelicidin family of cationic antimicrobial peptides in humans has been shown to exhibit a wide variety of biological actions in addition to its antimicrobial activity. However, the lymphangiogenic effect of LL-37 has not been elucidated yet. In this study, we examined the effects of LL-37 on lymphangiogenesis and evaluated the underlying molecular mechanisms. LL-37 treatment significantly increased the migration and tube-like formation of human dermal lymphatic microvascular endothelial cells (HDLECs) and promoted the expression of lymphangiogenic factor in HDLECs. Treatment with LL-37 increased phosphorylation of ERK and Akt proteins in HDLECs, and pretreatment with ERK and Akt inhibitors significantly blocked the LL-37-induced HDLEC migration and tube-like formation. Furthermore, to investigate the involvement of formyl peptide receptor-like 1 (FPRL-1) signaling in LL-37-induced lymphangiogenesis, HDLECs were treated with an FPRL-1 antagonist. Pretreatment with the FPRL-1 antagonist inhibited LL-37-induced phosphorylation of ERK and Akt proteins and attenuated LL-37-induced HDLEC migration and tube-like formation. These data indicated that LL-37-induces lymphangiogenesis in lymphatic endothelial cells via FPRL1, and the activation of the ERK and Akt-dependent signaling pathways.